Shinshu Med J, 73(6) : 399～406, 2025

Early Prediction of Acute Kidney Injury after Pediatric Cardiac Surgery

Shunsuke NODA

Pediatric Intensive Care Unit, Nagano Children's Hospital

Background : Cardiac surgery-associated acute kidney injury (CS-AKI) following pediatric cardiac surgery is associated with increased postoperative mortality and prolonged pediatric intensive care unit (PICU) stay. Early diagnosis and intervention are therefore essential. We retrospectively evaluated whether CS-AKI could be predicted using perioperative blood parameters, cardiopulmonary bypass (CPB) data, and postoperative furosemide responsiveness.

Methods : This retrospective study included 238 patients admitted to the PICU of Nagano Children's Hospital between April 2020 and March 2024. Age, body surface area (BSA), preoperative and postoperative serum creatinine (sCr), blood urea nitrogen (BUN), sodium, potassium, chloride, albumin, postoperative bicarbonate, lactate, serum osmolality, CPB time, and postoperative furosemide responsiveness were compared between AKI and non-AKI groups. Variables showing significant differences were analyzed to identify predictors of AKI onset.

Results : Significant differences between the AKI and non-AKI groups were observed in age, BSA, ΔCr (postoperative sCr-preoperative sCr), ΔK, CPB time, time to furosemide administration, and urine volume in response to furosemide. Logistic regression analysis identified CPB time, ΔCr, and furosemide-induced urine output as the most relevant predictors. In contrast, furosemide administration timing, BSA, ΔK, and age were less predictive. Highly relevant data were assigned a score of 2, and others a score of 1. A total score ≥ 6 predicted AKI onset with 90.8 % sensitivity and 90.5 % specificity.

Conclusion : Perioperative clinical and laboratory parameters can predict CS-AKI within 24 hours after pediatric cardiac surgery. Integrating these findings with established AKI biomarkers may further enhance prediction accuracy. *Shinshu Med J 73 : 399—406, 2025*

(Received for publication June 30, 2025 ; accepted in revised form September 11, 2025)

Key words : cardiac surgery-associated acute kidney injury (CS-AKI), pediatric intensive care unit (PICU), cardiopulmonary bypass (CPB), pediatric, chronic kidney disease (CKD)

I Introduction

Acute kidney injury (AKI) may result from various causes and is associated with decreased survival and an increased risk of progression to chronic kidney disease (CKD). Currently, no definitive treatment exists once AKI develops ; therefore, early diagnosis is critical to prevent further deterioration. Management strategies focus on renal protection, including maintaining adequate organ perfusion and avoiding nephrotoxic agents. Many cases of AKI occur during the perioperative period. Cardiac surgery-associated acute kidney injury (CS-AKI) following pediatric cardiac surgery is associated with increased postoperative mortality and prolonged pediatric intensive care unit (PICU) stay[1]. The incidence of CS-AKI following pediatric cardiac procedures has been reported to range from 9.6 % to 52 %[2]. CS-AKI may result from multiple factors, including mechanical hemolysis induced by cardiopulmonary bypass (CPB), inflammatory

Corresponding author : Shunsuke Noda
Pediatric Intensive Care Unit, Nagano Children's Hospital
3100, Toyoshina, Azumino, Nagano 399-8288, Japan
E-mail : shunsuke-noda@nkodomo-hsp.jp

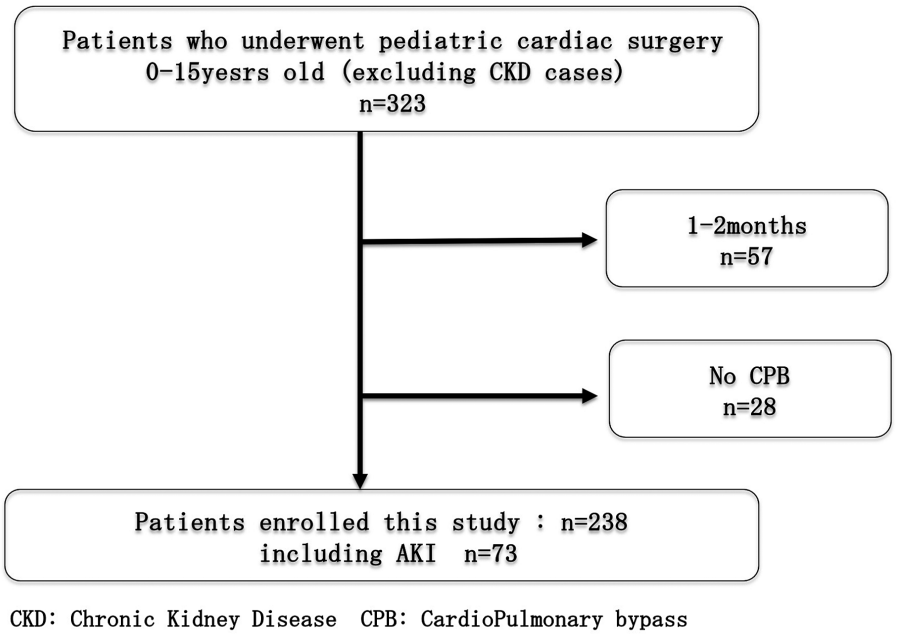

Fig. 1 Flow diagram of patient enrollment

Of the 323 pediatric patients aged 0–15 years who underwent cardiac surgery and were admitted to the PICU, 238 were included after excluding patients younge than 3 months and those who did not undergo CPB. Among these, 30 % developed AKI.

AKI : acute kidney injury, CPB : cardiopulmonary bypass, PICU : pediatric intensive care unit.

responses triggered by exposure to foreign materials, and renal ischemia secondary to hypoperfusion, all of which complicate postoperative management[3)4)].

Early identification of CS-AKI may allow timely initiation of renal-protective therapies and reduce the risk of complications. Although several studies have explored predictive approaches using biomarkers and artificial intelligence (AI)[5)-7)], biomarker availability varies across institutions, and AI-based prediction tools are not widely accepted in clinical practice. Consequently, there is no standardized set of markers to predict AKI onset in real-world pediatric settings. In this study, we analyzed perioperative variables, CPB duration, postoperative furosemide responsiveness, and age-to identify those significantly associated with AKI onset. We then evaluated whether a simple scoring system based on these factors could facilitate early clinical prediction of CS-AKI.

Ⅱ Methods

A Data collection

This was a single-center, retrospective observational study. Of 323 pediatric patients (aged 0–15 years) who underwent cardiac surgery and were admitted to the PICU at Nagano Children's Hospital between April 2020 and March 2024, 238 were included. Patients younger than 3 months or those who did not undergo CPB were excluded **(Fig. 1)**. The following clinical data were extracted from medical records : age, height, weight, body surface area (BSA), preoperative and postoperative serum creatinine (sCr), serum urea nitrogen (sBUN), potassium (K), sodium (Na), chloride (Cl), serum albumin (sAlb), postoperative bicarbonate, lactate, serum osmolality, intraoperative CPB time, furosemide-induced urine output (mL/kg/h) within 24 hours of PICU admission, and the timing of the first furosemide administration.

B Renal function assessment

AKI was diagnosed according to the Kidney Disease : Improving Global Outcomes (KDIGO) criteria[8)]. AKI was defined as a ≥ 1.5-fold increase in sCr within 72 hours postoperatively, consistent with stage 1 or higher. Both the AKI and non-AKI groups maintained a urine output of 2–3 ml/kg/h or greater within

24 hours after surgery, which did not meet the KDIGO criteria, and urine output was not used to diagnose AKI.

The following variables were compared between the AKI and non-AKI groups : preoperative and postoperative sCr, sBUN, serum K, Na, Cl, sAlb, postoperative bicarbonate, lactate, and serum osmolality ; Δx values (postoperative minus preoperative) for sCr (ΔCr), sBUN (ΔBUN), K (ΔK), Na (ΔNa), sAlb (ΔAlb) ; intraoperative CPB time ; aortic clamp time ; Time of first administration of furosemide (diuretic) within 24 hours after admission to the PICU when circulation was considered to have stabilized ; reactive urine volume (urine ; mL/kg/h) within 1 hour after the first administration of furosemide (initial dose 0.2–0.5 mg/kg/dose) ; and patient age, weight, height, and BSA.

C Statistical analyses

Continuous variables were expressed as median (IQR : Interquartile range).

All statistical analyses were performed using EZR statistical analysis software[9]. A two-sided significance level of $p<0.05$ was considered statistically significant. For continuous variables, normally distributed data were analyzed using the t-test, and non-normally distributed data using the Mann-Whitney U test. Variables using significant between-group differences were used to calculate AKI cutoff values via receiver operating characteristic (ROC) curve analysis. Logistic regression was then performed using these variables as predictors and AKI onset as the outcomes. The area under the ROC curve (AUC) was used to evaluate predictive performance. Variables with AUC > 0.75 were considered highly predictive and were assigned 2 points ; all other variables were assigned 1 point. The cumulative score was calculated to estimate the probability of AKI onset.

Ⅲ Result

A Patient characteristics and cutoff values of collected data

Among the 238 patients included in the analysis, 73 (30 %) developed moderate or severe AKI within 72 hours postoperatively. The length of stay in the intensive care unit was 9.8 days and 5.1 days in the AKI and non-AKI groups, respectively. The AKI group required more inotropes to maintain organ perfusion than the non-AKI group, and two patients underwent renal replacement therapy due to uncontrolled overflow despite fluid restriction. One patient died in the AKI group, but none in the non-AKI group. Significant differences between the AKI and non-AKI groups were observed for age, height, weight, BSA, ΔCr, ΔK, CPB time, aortic clamp time, time to first furosemide administration within 24 hours post-surgery, and furosemide-induced urine output **(Table 1)**. From these, seven variables were selected for further analysis : age, BSA, ΔCr, ΔK, Diuretic, Urine, and CPB time. Cutoff values for AKI prediction were determined from each variable **(Fig. 2)**.

Individually, these variables had an AUC of approximately 0.5–0.6, indicating limited discriminatory power and insufficient accuracy for AKI prediction when used alone.

B Logistic regression analysis and prediction model for AKI

Logistic regression analysis showed that odds ratios and P values indicated that extracorporeal circulation time, ΔCr, and furosemide-induced urine output were significantly associated with the development of AKI, whereas time to furosemide administration, body surface area, ΔK, and age did not show significant associations. **(Table 2)**.

Using logistic regression modeling, a total prediction score was calculated based on these variables. A cumulative score ≥ 6 yielded an AUC > 0.75 for predicting AKI onset. Patients were assigned 2 points if they met any of the following criteria : CPB time ≥ 165 minutes, ΔsCr ≥ 0.05 mg/dL, and furosemide-induced urine output ≤ 6.4 mL/kg/h. One point was assigned for meeting any of the following criteria : time to first furosemide administration ≤ 10 hours, BSA ≤ 0.50 m^2, age ≤ 24 months, and ΔK ≥ −0.4 **(Table 3)**.

Using a cutoff score of 6, the model demonstrated a sensitivity of 90.8 % and a specificity of 90.5 % for predicting postoperative AKI **(Fig. 3)**.

Table 1 Demographic, preoperative, and postoperative clinical data and characteristics of patients

	AKI (n = 73)	No AKI (n = 165)	*P* value
Age (mo)	23 (3～175)	36 (3～184)	＜0.05
Gender (male : female)	37 : 36	82 : 83	–
Weight (kg)	9.55 (4.0～82.0)	12 (3.27～52.5)	＜0.01
Height (cm)	80.8 (55～200)	88.7 (46.1～166.7)	＜0.05
BSA (m^2)	0.46 (0.25～2.13)	0.54 (0.224～1.48)	＜0.01
Pre BUN (mg/dL)	13 (6～32)	13 (3～26)	0.96
Post BUN (mg/dL)	11 (4～21)	11 (3～28)	0.90
ΔBUN	−3 (−14～11)	−4.75 (−14～0)	0.75
Pre Cr (mg/dL)	0.31 (0.11～0.81)	0.34 (0.19～0.76)	＜0.01
Post Cr (mg/dL)	0.34 (0.07～1.02)	0.34 (0.07～0.92)	0.82
ΔCr	0.06 (−0.1～0.35)	0.02 (−0.22～0.21)	＜0.01
Pre Na (mEq/L)	140 (129～143)	140 (133～144)	0.29
Post Na (mEq/L)	139 (131～143)	139 (132～145)	0.14
ΔNa	0 (−7～9)	−1 (−7～16)	0.74
Pre K (mEq/L)	4.2 (3.2～5.6)	4.2 (3.1～6.1)	0.75
Post K (mEq/L)	4.0 (2.6～5.7)	3.8 (2.9～6.2)	＜0.05
ΔK	−0.3 (−1.5～1.6)	−0.4 (−2.0～2.3)	＜0.05
Pre Cl (mEq/L)	106 (90～110)	106 (96～112) missing date n = 1	＜0.05
Post Cl (mEq/L)	104 (97～112)	105 (98～116) missing date n = 1	0.09
ΔCl	−1 (−9～8)	−1 (40～11)	0.14
Pre Alb (g/dL)	4.6 (2.6～5.3)	4.5 (3.5～5.5)	0.85
Post Alb (g/dl)	3.9 (2.2～5.4)	4.0 (2.2～5.7)	0.97
ΔAlb	−0.5 (−2.7～1.0)	−0.5 (−2.5～1.4)	0.59
Post HCO_3− (mEq/L)	23.3 (19.9～27.1)	23.7 (18.4～28.5)	0.08
Post Lactate (mg/dL)	2.0 (0.9～8.8)	2.0 (0.9−～7.5)	0.37
Post Osm	300 (283～491)	300 (282～556) missing date n = 1	0.50
CPB time (min)	168 (40～475)	120 (38～329)	＜0.01
Ao Clamp time (min)	90 (12～250) missing date n = 11	69 (10～215) missing date n = 34	＜0.01
Urine (ml/kg/h)	4.8 (0.0～21.0) missing date n = 7	7.4 (0.0～27.5) missing date n = 5	＜0.01
Diuretic time (hour)	9 (1～24)	11 (1～24)	＜0.05

AKI : acute kidney injury, BSA : body surface area, ΔBUN, ΔCr, ΔNa, ΔK, ΔCl : "Δ−"indicates the difference between preoperative and postoperative values of each parameter.
Pre, Post BUN, Cr, Na, K, Cl and Post Alb, HCO_3−, Lac, Osm : Pre− and Post− indicate preoperative and postoperative values of each parameter, respectively.
CPB time : intraoperative cardiopulmonary bypass time, Urine : first administration furosemide reaction urine output, Diuretic time : first administration time of furosemide after surgery.

Ⅳ Discussion

This study demonstrated that perioperative clinical data and laboratory findings can predict the onset of stage 1 or higher CS-AKI within 72 hours of pediatric cardiac surgery, with a predictive probability exceeding 75 %. Given that AKI develops within 3 days postoperatively in approximately 42 % of patients[1], early prediction-particularly within the first 24 hours-may facilitate timely interventions.

This study included only children aged ≥ 3 months, consistent with the applicability of the KDIGO AKI diagnostic criteria in this age group[10][11], and limited the population to patients undergoing CPB, where CS-AKI most commonly occurs[1].

In this cohort, CS-AKI was more frequently observed in younger children with lower body size, prolonged CPB duration, and diminished postoperative response to furosemide-especially when administered early. Known risk factors for CS-AKI have in-

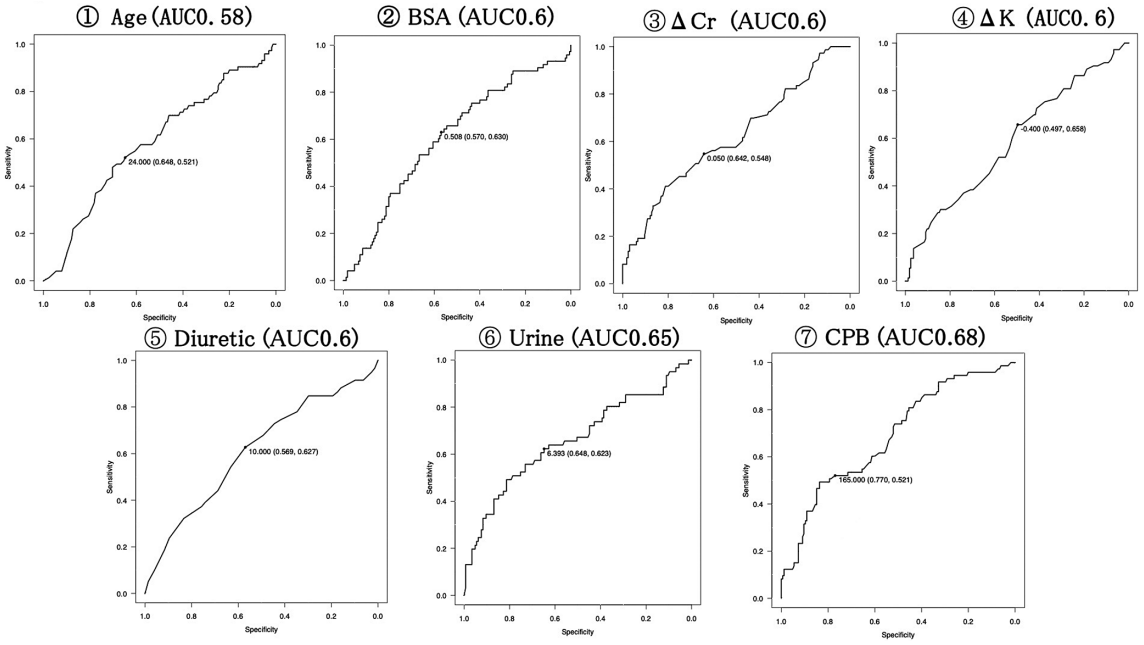

Fig. 2　Cutoff values for AKI onset

The following cut-off values were determined : CPB time ≥ 165 minutes, ΔsCr ≥ 0.05 mg/dL, furosemide-induced urine output ≤ 6.4 mL/kg/h, time to first furosemide administration ≤ 10 hours, BSA ≤ 0.50 m^2, age ≤ 24 months, and ΔK ≤ −0.4.

AKI : acute kidney injury, AUC : area under the curve, BSA : body surface area, CPB : cardiopulmonary bypass, ΔK : postoperative serum potassium minus preoperative serum potassium, ΔsCr : postoperative serum creatinine minus preoperative serum creatinine.

Table 2　Logistic regression analysis of predictors for AKI

	Odds ratio	95 % CI (Low)	95 %Cl (high)	*P* Value
Age	0.988	0.965	1.010	0.308
ΔCr	9730	56.50	1680000	＜0.01
ΔK	0.934	0.490	1.780	0.835
Diuretic	0.943	0.886	1.000	0.067
Urine	0.885	0.813	0.963	＜0.01
BSA	1.300	0.033	51.70	0.888
CPR	1.010	1.010	1.020	＜0.01

AKI : acute kidney injury, BSA : body surface area, CPB cardiopulmonary bypass, ΔCr : postoperative serum creatinine minus preoperative serum creatinine, ΔK : postoperative serum potassium minus preoperative serum potassium, Urine : first administration furosemide reaction urine output, Diuretic time : first administration time of furosemide after surgery,
95 %CI : confidence interval.

clude renal hypoperfusion, impaired renal tubular function, exposure to nephrotoxic agents, age ≤ 2 years, low birth weight, complex congenital heart defects, prolonged CPB, low cardiac output syndrome, sepsis, and systemic inflammatory response syndrome (SIRS) during CPB[12]. Previous studies have also identified CPB duration＞180 minutes and deep hypothermic circulatory arrest as independent risk factors for AKI[13], and prolonged surgery has been similarly associated with CS-AKI risk[14]. In the present study, patients with CPB duration ≥ 165 minutes, age ≤ 24 months, and low BSA were more likely to develop CS-AKI, which is consistent with these earlier findings.

Chawla et al. introduced the furosemide stress test

Table 3　Scoring system for prediction of AKI onset

A	CPB time ≧165 minutes (2 : 45)
	Postoperative-preoperative Cr (ΔCr) ≧0.05
	Furosemide reaction urine≦6.4 ml/kg/h or less
B	First administration of furosemide within 10 hours after surgery
	BSA≦0.50
	Postoperative-preoperative sK (ΔK) ≧-0.4
	Age≦24months

A : 2points, B : 1points

#A score of 2 was assigned for any criterion in A (strong predictors), and a score of 1 for meeting any criterion in B (weaker predictors). The total score for was used to calculate the probability of AKI onset.
AKI : acute kidney injury, BSA : body surface area, CPB : cardiopulmonary bypass, ΔCr : postoperative serum creatinine minus preoperative serum creatinine, ΔK : postoperative serum potassium minus preoperative serum potassium.

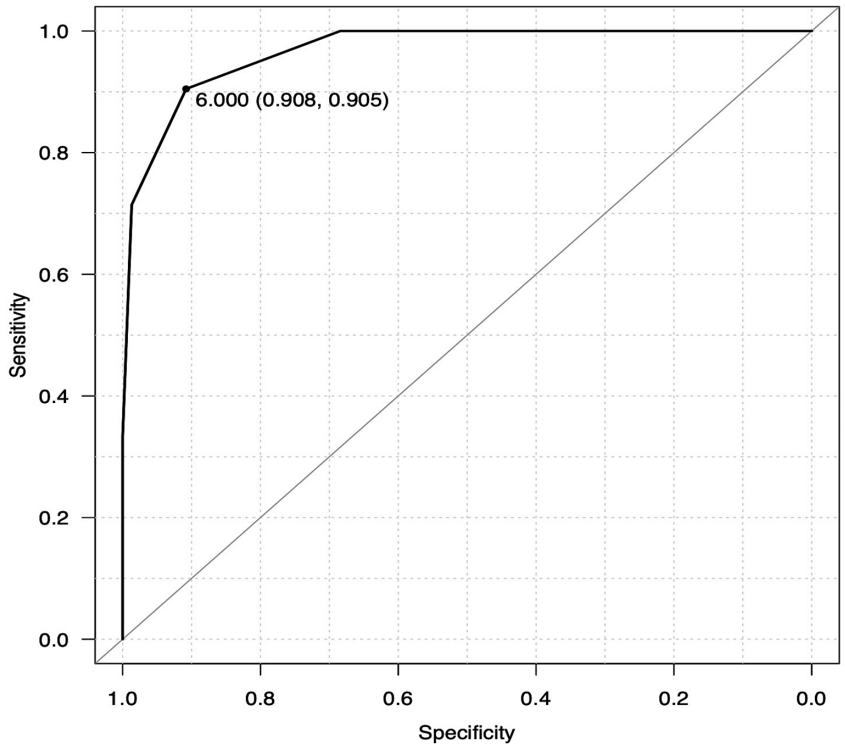

Fig. 3　The score of explanatory variables that satisfy AUC>0.75 of AKI onset prediction probability by logistic regression analysis

Logistic regression-based scoring model for predicting AKI onset with AUC>0.75.
A total score ≥ 6 yielded a specificity of 90.8 % and a sensitivity of 90.5 % for predicting AKI onset. The AUC was 0.968 (95 % CI 0.937-0.999).
AKI : acute kidney injury, AUC : area under the curve, CI : confidence interval.

(FST) as a method to predict AKI onset. In adult patients, a single intravenous dose of 1.0-1.5 mg/kg furosemide yielding ≤ 200 mL urine output within 2 hours demonstrated a sensitivity of 87.1 % and specificity of 84.1 % for predicting AKI[15]. Subsequent studies have confirmed that FST has strong diagnostic performance for early AKI, particularly in forecasting the need for renal replacement therapy[16].

Among pediatric patients undergoing cardiac surgery, reduced urine output at 2 and 6 hours post-furosemide administration has been significantly associated with AKI onset[17]. Kajiwala et al. administered furosemide (0.8–1.2 mg/kg/dose) to 568 infants within 8–24 hours post-CPB and reported that diminished diuretic response was a strong predictor of AKI[18].

In our study, the initial furosemide dose was typically 0.2–0.5 mg/kg, and a response of ≤ 6.4 ml/kg/h within 1 hour after administration was associated with CS-AKI. Although we did not assess the dose-response relationship, postoperative management protocols were consistent during the study period, minimizing variability. Notably, furosemide was often withheld during the early postoperative period due to increased vascular permeability and reduced intravascular volume following CPB and surgery, which necessitates cautious fluid management. However, in select cases-such as those with compromised cardiac function or signs of volume overload-early diuretic use (within 10 hours postoperatively) was considered, potentially reflecting early-stage CS-AKI.

This study has some limitations. It was a retrospective, single-center analysis based on medical record review. Although changes in perioperative care could introduce bias, no major modifications to CPB management or overall treatment protocols occurred during the study period, and we believe the risk of systemic bias was minimal.

V Conclusion

This study identified perioperative variables significantly associated with AKI and evaluated their predictive value using cutoff thresholds and multivariate analysis. The onset of AKI within 72 hours following pediatric cardiac surgery can be predicted within 24 hours postoperatively, with a sensitivity of 90.8 % and a specificity of 90.5 %. Early identification of high-risk patients may enable timely therapeutic intervention and potentially prevent AKI progression. Furthermore, prediction accuracy could be enhanced by combining this model with established AKI biomarkers.

Statements and Declarations

Competing Interests

The author declare that they have no competing interests.

Ethics approval

This study was approved by the Nagano Prefectural Children's Hospital Ethics Committee (approval number S-05-20) and was published on the hospital website as an opt-out study.

Data availability

All data generated or analysed during this study are included in this published article.

Author contributions

Author contributed to the study conception and design.

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（2025. 6. 30 received ; 2025. 9. 11 accepted）